Identification of Human Embryonic Progenitor Cell Targeting Peptides Using Phage Display.

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Public Summary:

Scientific Abstract:
Human pluripotent stem (hPS) cells are capable of differentiation into derivatives of all three primary embryonic germ layers and can self-renew indefinitely. They therefore offer a potentially scalable source of replacement cells to treat a variety of degenerative diseases. The ability to reprogram adult cells to induced pluripotent stem (iPS) cells has now enabled the possibility of patient-specific hPS cells as a source of cells for disease modeling, drug discovery, and potentially, cell replacement therapies. While reprogramming technology has dramatically increased the availability of normal and diseased hPS cell lines for basic research, a major bottleneck is the critical unmet need for more efficient methods of deriving well-defined cell populations from hPS cells. Phage display is a powerful method for selecting affinity ligands that could be used for identifying and potentially purifying a variety of cell types derived from hPS cells. However, identification of specific progenitor cell-binding peptides using phage display may be hindered by the large cellular heterogeneity present in differentiating hPS cell populations. We therefore tested the hypothesis that peptides selected for their ability to bind a clonal cell line derived from hPS cells would bind early progenitor cell types emerging from differentiating hPS cells. The human embryonic stem (hES) cell-derived embryonic progenitor cell line, W10, was used and cell-targeting peptides were identified. Competition studies demonstrated specificity of peptide binding to the target cell surface. Efficient peptide targeted cell labeling was accomplished using multivalent peptide-quantum dot complexes as detected by fluorescence microscopy and flow cytometry. The cell-binding peptides were selective for differentiated hPS cells, had little or no binding on pluripotent cells, but preferential binding to certain embryonic progenitor cell lines and early endodermal hPS cell derivatives. Taken together these data suggest that selection of phage display libraries against a clonal progenitor stem cell population can be used to identify progenitor stem cell targeting peptides. The peptides may be useful for monitoring hPS cell differentiation and for the development of cell enrichment procedures to improve the efficiency of directed differentiation toward clinically relevant human cell types.